representing 6 different cancers, namely, colon, ovary, prostate, breast, lung and leukemia. Further SEQ ID NO: 9-12 were tested on 8 different human tumor cell lines representing 7 different cancers, namely, oral, stomach, colon, glioblastoma, breast, larynx, and lung.

The compounds have been tested on sufficiently large number of cancers, which include cancers of different types such as adenocarcinoma, squamous cell carcinoma, cancer of the central nervous system and leukemia. Since all the tested compounds show cytotoxic activity on all the cell lines tested, it is reasonable to believe that these compounds would show anticancer activity on other adenocarcinomas (such as cancers of the gastrointestinal tract, prostate, renal, hepatic, bladder, oesophagus, etc), squamous cell cancers (head and neck, skin, non small cell lung cancer, etc), cancers of central nervous system (neuroblastomas, astrocytomas, meduloblastomas, etc) and other leukemias.

In addition, further evidence is provided in which pharmaceutical compositions of the peptides, including the dosage amount and protocols of using a therapeutically effective pharmaceutical composition are shown for treating cancer in general. The invention provides a method for treating a mammal (including a human being) afflicted with cancer. The types of cancer that may be treated include, but are not necessarily limited to, cancers of breast, pancreas, stomach, oral, lung, colon, ovary leukemia, prostate, glioblastoma, and larynx.

The method of this invention comprises, consists of, or consists essentially of administering systemically to the mammal a therapeutically effective dose of peptide SEQ ID NO : 3, SEQ ID NO : 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO : 7, SEQ ID NO : 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, or SEQ ID NO : 13. A dose of the peptide ranging between 0.25 μg /Kg. BWt to 500 μg /Kg. BWt is preferred. More preferably the doesage is in the range of

10μg /Kg. BWt to 200 μg /Kg. BWt. However, the dose is dependent on the effects sought, the manner of administration, the peptide selected, and the cancer being treated. Systemic administration refers to oral, rectal, nasal, transdermal, and parental (i.e., intramuscular, intravenous, and subcutaneous). In accordance with good clinical practice, it is preferred to administer the composition at a dose that will produce anticancer effects without causing undue harmful side effects. The composition may be administered either alone or as a mixture with other therapeuticor chemotherapeutic agents.

The composition may optionally and preferably contain pharmaceutically acceptable diluents, excipients, solvents, binders, stabilizers, and the like. Such diluents may include: RPMI 1640, buffered saline, isotonic NaCl, Ringer's solution, water, distilled water, polyethylene glycol (neat or in water), 2% Tween in water, dimethylsulfoxide to 50% in water, propylene glycol (neat or in water), phosphate buffered saline, balanced salt solution, glycerol, and other conventional fluids that are suitable for intravenous administration. Pharmaceutical compositions which provide from about 0.1 to 10.0 mg of the composition per unit dose are preferred and are conventionally prepared as tablets, lozenges, capsules, powders, aqueous or oily suspensions, syrups, elixirs, and aqueous solutions. The nature of the pharmaceutical composition employed will, of course, depend on the desired route of administration.

In addition to the protocols described on page 8, lines 1-27, a method of treatment of cancer in mammals in general by administering an effective amount of the polypeptides claimed are described which shows that the peptides claimed individually are useful as a pharmaceutical composition by administering as an active ingredient a therapeutically effective amount of the peptide to treat cancer in mammals including humans in the manner claimed in the instant invention.

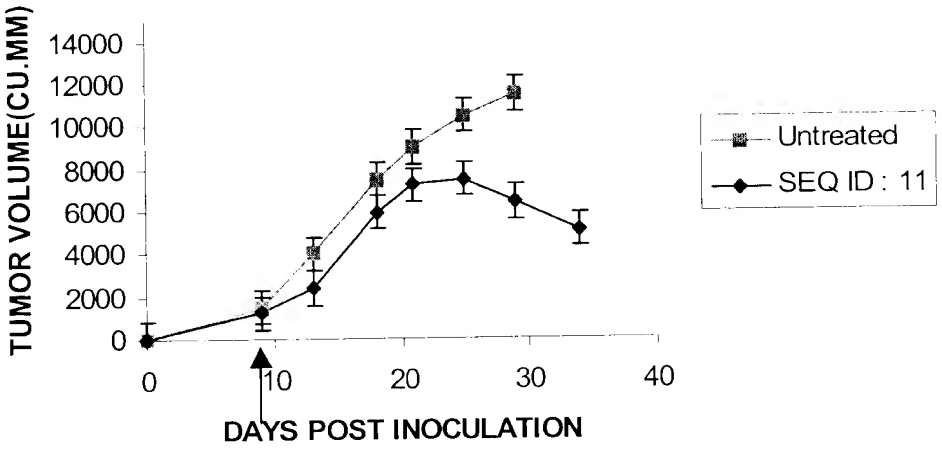
Example

Protocol and method of treating an animal with cancer using SEQ ID : 11

Primary tumor cells of colon adenocarcinoma (PTC) xenografts were initiated in Balb/c athymic mice by subcutaneous inoculation of a single cell suspension of PTC cells(15×10^6 cells/100 µL). When the average tumor volumes, as measured using a vernier caliper, were between 400 – 800 mm^3 , treatment was initiated on the tumor bearing animals which were divided into two groups of three animals each including one untreated control group. SEQ ID NO : 11 was prepared at a concentration of 42.5 µg/ml by solubilizing the said amount of peptide in water. Alternately, the peptide may be solubilized in any of the other solvents commonly used and listed above. The solubilized peptide was administered intravenously at a dose of 4.25 µg/100 µL twice a day. The antitumor activity was monitored by measuring tumor volumes every fourth day using the formula W*W*L*0.4 (W = smaller dia, L = larger dia). It may be noted that all control (untreated) animals died by day 29 post treatment. The percentage inhibition of tumor growth was calculated using the formula (1- tumor volume(treated) / tumor volume (control))* 100.

The following figure shows the pattern of tumor growth till day 21 in treated and untreated animals. The percentage inhibition of tumor growth caused by SEQ ID NO : 11 as compared to untreated on day 18 was 53%.

INVIVO ANTITUMOR EFFECT OF SEQ ID : 11(Dose x = 8.5 ug/day) ON PTC XENOGRAFTS



According to MPEP 2107.03 data from *in vitro* testing is generally sufficient to support therapeutic utility. There is no decisional law that requires an applicant to provide human clinical data. It is understood in the art that in order to proceed with *in vivo* screening there must be positive results in *in vitro* screens. The Examiner's attention is drawn to the existence of the Developmental Therapeutics Program of the National Cancer Institute. Molecules are screened in an aim to discover specific anticancer agents. The molecules are first subjected to *in vitro* screening followed by *in vivo* screening on select tumor xenografts. The details of DTP are set out in the a paper titled "The National Cancer Institute: Cancer Drug Discovery and Development Program" by Grever et al. in Seminars in Oncology Vol. 19, No. 6 (December), 1992, p622-638 wherein it is clearly indicated that molecules are subject to *in vitro* screen prior to testing in *in vivo* models.

Therefore, since applicants have established that the peptides of this invention are effective against a wide range of types of cancer and that efficacy in *in vitro* models is predictive of efficacy

in *in vivo* systems, it is respectfully requested that this rejection be withdrawn

The Examiner has rejected Claims 1-14 under 35 USC 112, second paragraph as being indefinite. Applicants respectfully traverse this rejection.

The Examiner states that Claim 1 is indefinite because it does not recite a function or activity of the peptide. It is not necessary to include in a compound claim the function or activity of the compound. All that is required is that the specification disclose a utility for the claimed invention. The specification discloses that the peptides of claim 1 can be used to treat cancer. Therefore, it is respectfully requested that this rejection be withdrawn.

The Examiner has rejected Claims 13 and 14 as being indefinite because according to the Examiner it is not clear what is meant by the terms "effective amount" and "chemotherapeutic."

As explained on page 8, lines 22-24 of the specification, "an effective amount" means that amount of a drug or pharmaceutical agent that will elicit the biological or medical response of a tissue, system, animal or human that is being sought.

The term "chemotherapeutic compound" is understood by those in the art to include compounds which can be used to treat cancer. See page 4, lines 7-9 of the specification. One skilled in the art would consider drugs such as Paclitaxel, Taxotere, Etoposide, Doxorubicin, 5-fluorouracil, Methotrexate, Vincristine, Vinblastine, Cisplatin, Carboplatin, Cyclophosphamide, Cytarabine, Ifosfamide, Irinotecan and Topotecan to be chemotherapeutic compounds.

Therefore it is respectfully requested that this rejection be withdrawn.

Applicants submit that the present application is in condition for allowance and favorable consideration is respectfully requested.

Respectfully submitted,

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MARKED-UP COPY

Please replace the second full paragraph on page 11 with the following:

- - The resulting crude peptide was purified by preperative high performance liquid chromatography (HPLC) using a [LiChroCART] LICHROCART® C,8 (250. Times. 10) (reverse phase C-18 column) reverse phase column (Merck, Darmstadt, Germany) on a Preparative HPLC system (Shimadzu Corporation, Japan) using a gradient of 0.1 % TFA in acetronitrile and water. The eluted fractions were reanalyzed on Analytical HPLC system (Shimadzu Corporation, Japan) using a C18 [LiChrospherg] LICHROSPHERG®, WP-300 (300 [LiChrospherg] X 4) (reverse phase C-18 column) reverse-phase column. Acetronitrile was evaporated and the fractions were lyophilized to obtain the pure peptide. The identity of each peptide was confirmed by electron-spray mass spectroscopy.- -